**COMPARATIVE CHANGES IN PURKINJE FIBER CONDUCTION VELOCITY: POSSIBLE ROLE IN SPECIES DIFFERENCES IN ECG FROM "MOUSE TO WHALE".**

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Interspecies differences in ECG intervals were discovered 60 years ago. An unexplained finding has been the brevity of the PR interval in large mammals (e.g. whales, elephants) relative to their body size. We hypothesized that part of the species differences in PR interval might be due to progressive changes in conduction velocity (cond vel.) in the His-Purkinje system. Microelectrode techniques were used to study the active and passive properties of cat, dog, and sheep Purkinje fibers (PF). Comparative changes in PF cond vel. correlated with heart size (see Table): cond vel. in sheep was 1.7 and 2.4 times faster than dog and cat respectively. Changes in cond vel. were not associated with species differences in transmembrane potential ($V_m$), action potential amplitude (APA) or upstroke velocity ($V_{max}$) (mean ± SE):

| Species | $V_m$ | APA | $V_{max}$ | Cond Vel. | (n) |
|---|---|---|---|---|---|
| Cat | -84 ± 1 | 119 ± 1 | 596 | 1.44 ± .15 | 3 |
| Dog | -87 ± 1 | 123 ± 1 | 528 ± 19 | 2.09 ± .09 | 9 |
| Sheep | -85 ± 1 | 124 ± 1 | 614 ± 85 | 3.46 ± .17 | 7 |

Passive determinants of cond vel. were measured by cable analysis. The space constant was larger in sheep PF than in dog (2.21 vs 1.72 mm); membrane time constants were not different. The results suggest: 1) PF cond vel. increases with species size; and 2) species differences in space constant and hence axial resistance may be a significant factor in comparative changes in conduction.

**THE PROTECTIVE POTENTIAL OF COLLATERALS DEPENDS ON THE TIME OF THEIR DEVELOPMENT.**

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Studies assessing the protective potential of collateral flow days or weeks after acute myocardial infarction have yielded conflicting results. We assessed change of left ventricular ejection fraction (ΔEF) from pre-intervention to day 10-14 in a randomized reperfusion trial (n=393). In 30 patients total occlusion of the infarct vessel persisted acutely and by day 10-14 angiography. There was collateral flow at acute angiography in 11 patients (acute collaterals); collaterals were not visible at acute angiography but had developed by day 10-14 angiography in 17 patients (delayed collaterals); collaterals were never seen in 2 patients (no collaterals).

| Collaterals | Acute EF | Day 10-14 EF | pΔEF |
|---|---|---|---|
| Acute | 53±9% | 55±7% | NS |
| Delayed | 44±16% | 39±12% | <0.01 |
| None | 42±8% | 34±5% | |

The difference in day 10-14 EF between patients with acute collaterals and those without acute collaterals was significant ($p < 0.01$); (acute EF difference $p < 0.08$). Conclusion: The collaterals visible at acute angiography in 36% of patients with total occlusion preserve EF during acute infarction and prevent a decrease of EF during the healing phase. The collaterals which develop with delay in 57% of patients with persistent occlusion do not protect EF.

## Wednesday, March 21, 1990
## 2:00PM-3:30PM, Room 16
## Coronary Artery Disease, Ischemia and Myocardial Function

**DOES VESSEL PATENCY AT THE TIME OF HOSPITAL DISCHARGE FOLLOWING THROMBOLYTIC THERAPY PREDICT SURVIVAL?**

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We assessed the prognostic value of a patent infarct related artery at the time of hospital discharge following myocardial infarction.

In the Western Washington Emergency Room Tissue Plasminogen Activator (tPA) Study, 160 patients received tPA on admission (143±60 minutes after the onset of symptoms) for acute myocardial infarction (AMI). Of 112 patients with pre-discharge ventricular and coronary angiograms, 109 had one year follow-up. At 5±2 days post AMI, 78% had a patent infarct related artery, and the ejection fraction (EF) was 52±11%. Within 15 days post AMI, 34% had a revascularization procedure performed. Over the one year of follow-up, 6 patients died. By Cox regression analysis, survival was predicted by the EF but not by infarct artery patency, infarct location or revascularization.

Thus, survival in patients with AMI depends on the level of LV function achieved after thrombolytic therapy with tPA. The patency of the infarct related artery at the time of discharge does not appear to give prognostic information.

**A RANDOMIZED CONTROLLED TRIAL OF ALLOPURINOL IN COMPLEX CORONARY BYPASS SURGERY**

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Experimental evidence indicates that allopurinol (allo) reduces cytotoxic free radicals formed during myocardial ischemia and reperfusion. This study evaluated the effect of allo on cardiac performance and early mortality following complex coronary bypass surgery. Allo (3.5 mg/Kg., given 4 hours before and the evening before surgery) or placebo was administered to 169 patients. Randomization produced groups evenly matched for these surgical risk factors (SRF): insulin diabetes, female gender, pre-operative renal dysfunction, previous surgery or PTCA, ejection fraction under .40, age over 70, multiple coronary endaterectomy, previous myocardial infarction. The allo group had an average of 2.64 SRF; the placebo group 2.75 SRF. Intermittent ischemic arrest with 30-33 degree C. total body hypothermia was used. Total ischemic times were: placebo 131.7, +/- 50; allo 130.2 +/- 47 minutes. Hospital mortality in the placebo group was 14/80 (17.5%), in the allopurinol group 4/89 (4.5%), p=0.014. Cardiac performance was significantly better in the allopurinol group. Eleven (12%) of the allo group versus 21(26%) of the placebo group required mechanical and pharmacological support to sustain a cardiac index over 2.0, p=0.021. No undesirable side effects were observed.

SUMMARY Allo appears to improve cardiac performance following complex coronary bypass surgery. We now administer allo to all patients undergoing bypass surgery unless specifically contraindicated.